UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,426	01/30/2006	John W. Phillips	RS0212	1907

7590 06/23/2009

R. DOUGLAS BRADLEY
MERCK & CO. INC. PATENT DEPT
P.O. BOX 2000
RY60-30
RAHWAY, NJ 07065-0907

EXAMINER	
ARCHIE, NINA	
ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,426	PHILLIPS, JOHN W.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *22 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13,15-17,19-23 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,13,15-17,19-23 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 12-22-08. Claims 1-11, 13, 15-16, 17, 19, 20-21, 22, 23, 25-30 are currently pending and under examination.

Rejections Withdrawn

2. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Rejections to claims 4 and 20 under 35 U.S.C. 102(e) as being unpatentable over Dixon et al US Patent No. 6828092 B1 Date December 7, 2004 US Filing Date January 12, 1998 is withdrawn in light of applicant's amendment thereto.

b) Rejections to claims 1-11, 13, 15, 17, 19-23, and 25-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Dixon et al US Patent No. 6828092 B1 Date December 7, 2004 US Filing Date January 12, 1998 in view of Ashby et al WO/2000/58521 Date October 5, 2000, Phillips, J. US Patent No: 7022481B2 Date April 4, 2006 US Filing Date December 19, 2002, and Contreras et al. WO/2001/02550A2 Date January 11, 2001 is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The rejections of claims 1-11, 13, 15, 17, 19, 20-23, and 25-30 are rejected under 35 U.S.C. 112, first paragraph for the reasons set forth in the previous office action. , as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant arguments:

Applicants arguments filed in response to the 35 U.S.C. 112, first paragraph, December 22, 2008 have been carefully considered, but not found to be persuasive for the reasons below.

Applicants argue that it is clear that homologs of YMR325 promoters are those YMR325 promoter sequences that have incorporated one or more nucleotide substitutions, additions or deletions, however, these sequence alterations do not substantially effect the ability of the promoter sequence to promote transcription of an operatively linked sequence when compared to the wild type YMR325 promoter that does not have any of the one or more nucleotide substitutions, additions or deletions (see, e.g., paragraph 0042, lines 4-12 and paragraph 0043 of the instant specification). Applicants state that promoters used in the claimed methods all retain substantially the same indicator function as the wild type YMR325 promoter. Applicants argue that one skilled in the art can easily discern if a YMR325 promoter that has one or more sequence alterations is within the scope of the claims by comparing its function to the YMR325 promoter sequence without such alterations and any of the assays described in the specification or know in the art at the time of filing to assay promoter function can be used. Applicant contends that structural information is provided (e.g., the sequence of the native YMR325 promoter) as well as functional information (e.g., the promoter's indicator properties) such that one skilled in the art could take the provided sequence and altered as described and then test to see if the described functional property remains.

Examiner's Response to Applicant's Arguments:

In response to applicant's statement in as set forth supra, Based on the limited number of homologs of YMR325 promoters disclosed in the specification, and that said homologs of YMR325 promoters were properly described is not persuasive. The limited number of species disclosed is not deemed to be representative of the genus encompassed by the instant claims. Furthermore although applicant amended claims, claims 1, 13, and 21 recites phrase "a promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions that do not effect the ability of the sequence to promote transcription of said operatively linked sequence in substantially the same manner as native YMR325W that does not comprise said one or more nucleotide substitutions, additions, or deletions", thus said recitation states the replacement

residue can be replaced with any amino acid residue and the term "homolog" is not defined in the specification, and does not have a precise meaning in the art, and is thus interpreted as reading upon any promoter possessing any degree of similarity to the specifically recited promoters, which thus represents a vast genus as stated in the previous office action.

Moreover, the specification is silent with regard to what constitutes recitation "in substantially the same manner" therefore claims directed to said recitation is unclear to interpret. The specification does not define nor sets forth the meaning to "in substantially the same manner". The specification also is silent with regard to what core structure needs to be present for the promoter to function as claimed. The specification does not disclose distinguishing and identifying features of a representative number of members of the genus of promoters to which the claims are drawn, such as a correlation between the structure of the promoter and its function as claimed, so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of promoters aforementioned above.

Moreover, Applicant is reminded that adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

As outlined previously, the claims are drawn to a method for determining whether a molecule affects the function or activity of a sterol biosynthesis pathway in a S. cerevisiae cell comprising: (a) contacting said cell with, or recombinantly expressing within said cell, said molecule; and (b) determining the amount of whether RNA expression or protein expression of a target polynucleotide sequence in said cell, said target polynucleotide being a sequence operatively linked to a promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions that do does not effect the ability of the sequence to promote transcription of said operatively linked sequence in substantially the same manner as native YMR325W that does not comprise said one or more nucleotide substitutions, additions or deletions; wherein an altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule as compared to a cell not contacted with said molecule indicates that said molecule does affect the function or activity of said sterol biosynthesis pathway (claim 1), wherein said

target polynucleotide sequence comprises a marker gene (claim 2), wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule is deceased as compared to a cell not contacted with said molecule (claim 3), wherein said target polynucleotide is operatively linked to a promoter native to S. cerevisiae gene YMR325W (claim 4), wherein RNA expression of said polynucleotide is changed in said cell contacted with said molecule as compared to a cell not contacted with said molecule (claim 5), wherein protein expression of said polynucleotide is changed in said cell contacted with said molecule as compared to a cell not contacted with said molecule (claim 6), wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule is increased as compared to a cell not contacted with said molecule (claim 7), wherein the S. cerevisiae cell is a cell that recombinantly expresses said target polynucleotide sequence (claim 8), wherein said contacting is carried out in a liquid high throughput-like assay (claim 9), wherein said contacting is carried out in a solid plate halo assay (claim 10), wherein said contacting carried out in an agar overlay assay (claim 11); a method for monitoring activity of a sterol biosynthesis pathway in a S. Cerevisiae cell exposed to a molecule comprising: (a) contacting said cell with, or recombinantly expressing within said cell, said molecule; and (b) determining the amount of RNA expression or protein expression of a target polynucleotide sequence in said cell is changed in step (a) relative to expression of said target polynucleotide sequence in the absence of said molecule, said target polynucleotide sequence being regulated by a promoter native to a S. cerevisiae YMR325W gene or a YMR325W promoter sequence homolog-comprising one or more nucleotide substitutions, additions or deletions that do does not effect the ability of the sequence to promote regulated transcription of said target polynucleotide sequence in substantially the same manner as native YMR325W that does not comprise said one or more nucleotide substitutions, additions or deletions; and wherein an altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule as compared to a cell not contacted with said molecule indicates that said function or activity of said sterol biosynthesis pathway is altered (claim 13), wherein said cell is contacted with said molecule step (a) comprises contacting said cell with said molecule (claim 15), wherein said molecule is recombinantly expressed in said cell (claim 17); wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule

is increased as compared to a cell not contacted with said molecule indicates of said sterol biosynthesis pathway is inhibited (claim 19), wherein said target polynucleotide sequence comprises S. cerevisiae YMR325W (claim 20); a method for identifying a molecule that modulates expression of a sterol biosynthesis pathway target polynucleotide sequence comprising: (a) recombinantly expressing in a S. cerevisiae cell, or contacting a S. cerevisiae cell with, at least one candidate molecule; and (b) measuring RNA or protein expression of a target polynucleotide sequence in said cell, said target polynucleotide sequence being regulated by a promoter native to a S. cerevisiae YMR325W gene or a YMR325W promoter sequence homolog-comprising one or more nucleotide substitutions, additions or deletions that does not effect the ability of the sequence to promote regulated transcription of said target polynucleotide sequence in substantially the same manner as native YMR325W that does not comprise said one or more nucleotide substitutions, additions or deletions; wherein an increase or decrease in expression of said target polynucleotide sequence relative to expression of said target polynucleotide sequence in the absence of said candidate molecule indicates that said candidate molecule modulates expression of said sterol biosynthesis pathway target polynucleotide sequence (claim 21), wherein said promoter comprises SEQ ID NO: 3 or a SEQ ID NO: 3 homolog-comprising one or more nucleotide substitutions, additions or deletions that do not effect the ability of the sequence to promote transcription of said operatively linked sequence (claim 22), wherein said marker gene is selected from the group consisting of green fluorescent protein, red fluorescent protein, blue fluorescent protein, luciferase, LEU2, LYS2, ADE2, TRP 1, CAN 1, CYH2, GUS, CUP 1 and chloramphenicol acetyl transferase (claim 23), wherein said molecule is selected from the group consisting of natural products, proteins, and small molecules (claim 25), wherein said molecule is purified (claim 26), wherein said molecule is not substantially purified (claim 27), wherein said contacting comprises incubating said cell with a second cell that produces said molecule (claim 28), wherein said molecule is released by said second cell (claim 29), wherein said molecule is secreted by said test second cell (claim 30).

Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

To fulfill the written description requirements set forth under 35 USC § 112, first

paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention.

To adequately describe the genus of promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions. Applicant must adequately describe homolog forms that operatively link to a target polynucleotide. The specification, however, does not disclose distinguishing and identifying features of a representative number of members of the genus of promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions to which the claims are drawn, such as a correlation between the structure of a promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions and its function (operatively link to a target polynucleotide to determine RNA expression), so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus aforementioned above.

The specification discloses 162 experiments/profiles of the sterol branch were used to evaluate the performance of the YMR325W gene reporter in terms of its sensitivity and specificity as an indicator of inhibition of sterol biosyntheses and the expression of the YMR325W gene reporter was measured in 1642 out of the 1647 experiments in the GRM data set (see pg. 34). The specification disclose results displaying that induction of the upregulation of the YMR325W gene reporter is a highly specific indicator of inhibition of the sterol biosynthesis pathway (see pg. 35 paragraphs 1-2). The specification disclose both Miconazole and Lovastatin inhibited the growth of the lawn of the YMR325W gene reporter strain in "Halo Assay" (see pgs. 36-37). These disclosures do not provide adequate description of the claimed genus of genus of an a promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions.

Moreover, the specification fails to disclose which amino acid residues are essential to

the function of the amino acid or which amino acids might be replaced so that the resultant amino acid retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant amino acid retains the activity of its parent. Therefore, since the specification fails to adequately describe at least a substantial number of members of the genus of aforementioned above to which the claims are based; the specification fails to adequately describe at least a substantial number of members of the claimed genus of an a promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions possessing the function of operatively linking a target nucleotide to determine RNA expression.

Moreover, the specification is silent with regard to what constitutes recitation "in substantially the same manner" therefore claims directed to said recitation is unclear to interpret. The specification does not define nor sets forth the meaning to "in substantially the same manner". The specification also is silent with regard to what core structure needs to be present for the promoter to function as claimed. The specification does not disclose distinguishing and identifying features of a representative number of members of the genus of promoters to which the claims are drawn, such as a correlation between the structure of the promoter and its function as claimed, so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of promoters aforementioned above.

PEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See

Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's

sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of an aforementioned above and its function (operatively link to a target polynucleotide to determine RNA expression), the skilled artisan could not immediately recognize or distinguish members of the claimed genus aforementioned above the function operatively linked to a target polynucleotide. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of genus of promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions in the claimed invention to possess the function operatively linking a target polynucleotide to determine RNA expression is not deemed representative of the genus of a promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions to which the claims refer and therefore the claimed invention is not properly disclosed.

Claim Rejections Maintained- 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. The rejection of claims 1-3, 5-9, 13, 15, 17, 19, 21, 23, 25, and 28-30 under 35 U.S.C. 102(e) as being unpatentable over Dixon et al US Patent No. 6828092 B1 Date December 7, 2004 US Filing Date January 12, 1998 are maintained for the reasons set forth in the previous office action.

Applicant arguments:

Applicants arguments filed in response to the 35 U.S.C. 112, first paragraph, December 22, 2008 is carefully considered, but not found to be persuasive for the reasons below.

Applicant respectfully disagrees with that characterization for the reasons stated supra. Applicant contends that the claims as currently pending encompass YMR325W promoters and homologs that promote transcription substantially as does wild type YMR325W not every conceivable promoter in nature.

Applicant argues that each and every limitation of the claimed invention be disclosed in a single prior art reference. In re Paulsen, 30 F.3d 1475, 31 USPQ2d 1671 (Fed. Cir. 1994) Applicant contends that the acetoacetyl CoA thiolase gene promoter used in Dixon is not equivalent to a YMR325W homolog.

Examiner's Response to Applicant's Arguments:

In response to applicant's statement in as set forth supra, Based on the limited number of homologs of YMR325 promoters disclosed in the specification, and that said homologs of YMR325 promoters were properly described is not persuasive. The limited number of species disclosed is not deemed to be representative of the instant claims. Furthermore although applicant amended claims, claims 1, 13, and 21 recites phrase "a promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions that do not effect the ability of the sequence to promote transcription of said operatively linked sequence in substantially the same manner as native YMR325W that does not comprise said one or more nucleotide substitutions, additions, or deletions", thus said recitation states the replacement residue can be replaced with any amino acid residue and the term "homolog" is not defined in the specification, and does not have a precise meaning in the art, and is thus interpreted as reading upon any promoter possessing any

degree of similarity to the specifically recited promoters, which thus the limitations of the claims have been met.

As outlined previously, the claims are drawn to a method for determining whether a molecule affects the function or activity of a sterol biosynthesis pathway in a S. cerevisiae cell (claim 1), a method for monitoring activity of a sterol biosynthesis pathway in a S. cerevisiae cell exposed to a molecule (claim 13), a method for identifying a molecule that modulates expression of a sterol biosynthesis pathway in a S. cerevisiae cell (claim 13) comprising:

(a) contacting said cell with, or recombinantly expressing within said cell, said molecule; and (b) determining the amount of whether RNA expression or protein expression of a target polynucleotide sequence in said cell, said target polynucleotide being a sequence operatively linked to a promoter native to S. cerevisiae gene YMR325W, or a YMR325W promoter sequence homolog comprising one or more nucleotide substitutions, additions or deletions that do does not effect the ability of the sequence to promote transcription of said operatively linked sequence in substantially the same manner as native YMR325W that does not comprise said one or more nucleotide substitutions, additions or deletions (claims 1, 13, and 21), wherein an altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule as compared to a cell not contacted with said molecule indicates that said molecule does affect the function or activity of said sterol biosynthesis pathway (claim 1), wherein an altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule as compared to a cell not contacted with said molecule indicates that said function or activity of said sterol biosynthesis pathway is altered (claim 13), wherein an increase or decrease in expression of said target polynucleotide sequence relative to expression of said target polynucleotide sequence in the absence of said candidate molecule indicates that said candidate molecule modulates expression of said sterol biosynthesis pathway target polynucleotide sequence (claim 21), wherein said target polynucleotide sequence comprises a marker gene (claim 2), wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule is deceased as compared to a cell not contacted with said molecule (claim 3), wherein RNA expression of said polynucleotide is changed in said cell contacted with said molecule as compared to a cell not contacted with said molecule (claim 5), wherein protein expression of said polynucleotide is

changed in said cell contacted with said molecule as compared to a cell not contacted with said molecule (claim 6), wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule is increased as compared to a cell not contacted with said molecule (claim 7), wherein the S. cerevisiae cell is a cell that recombinantly expresses said target polynucleotide sequence (claim 8), wherein said contacting is carried out in a liquid high throughput-like assay (claim 9), wherein said cell is contacted with said molecule step (a) comprises contacting said cell with said molecule (claim 15), wherein said molecule is recombinantly expressed in said cell (claim 17); wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule is increased as compared to a cell not contacted with said molecule indicates of said sterol biosynthesis pathway is inhibited (claim 19), wherein said promoter comprises SEQ ID NO: 3 or a SEQ ID NO: 3 homolog-comprising one or more nucleotide substitutions, additions or deletions that do not effect the ability of the sequence to promote transcription of said operatively linked sequence (claim 22), wherein said marker gene is selected from the group consisting of green fluorescent protein, red fluorescent protein, blue fluorescent protein, luciferase, LEU2, LYS2, ADE2, TRP 1, CAN 1, CYH2, GUS, CUP 1 and chloramphenicol acetyl transferase (claim 23), wherein said molecule is selected from the group consisting of natural products, proteins, and small molecules (claim 25), wherein said contacting comprises incubating said cell with a second cell that produces said molecule (claim 28), wherein said molecule is released by said second cell (claim 29), wherein said molecule is secreted by said test second cell (claim 30).

Dixon et al teach a method for the identification of agents which modulate sterol biosynthesis which method comprises contacting a test compound with a host cell comprising a DNA sequence which controls expression of a yeast acetoacetyl CoA thiolase gene operably linked to a reporter system thus modulation of sterol biosynthesis which regulates the transcription of the genes in the host cell leads to a detectable change in cell phenotype, and determining whether any such detectable change has occurred (see abstract) which correlates to a method for determining whether a molecule affects the function or activity of a sterol biosynthesis pathway in a S. cerevisiae cell comprising: (a) contacting said cell with, or

recombinantly expressing within said cell, said molecule; and (b) determining the amount of whether RNA expression or protein expression of a target polynucleotide sequence in said cell, said target polynucleotide being a sequence operatively linked to a promoter native to S. cerevisiae as YMR325W promoter sequence homolog/ a SEQ ID NO: 3 homolog-comprising comprising one or more nucleotide substitutions, additions or deletions that do does not effect the ability of the sequence to promote transcription of said operatively linked sequence in substantially the same manner as native YMR325W that does not comprise said one or more nucleotide substitutions, additions or deletions, wherein protein expression of said polynucleotide is changed in said cell contacted with said molecule as compared to a cell not contacted with said molecule.

Dixon et al teach a 5' flanking region of the ACoAT gene by cloning a 5' flanking region and fused it to a reporter gene (Escherichia coli (E. coli) b-galactosidase) and this result provide evidence that ACoAT activity is feedback regulated by sterol levels through regulation of gene transcription, and that at least some of the DNA elements which mediate this effect reside within the promoter region used to construct the reporter gene thus the effects of sterol biosynthesis inhibitors on reporter gene expression could, in theory, be due to effects on mRNA translation mediated by this sequence at the RNA level, rather than by effects on transcription (see column 6) which correlates to a method, wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule.

Dixon et al teach a method, wherein said target polynucleotide sequence comprises a marker gene (see columns 5-6), wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule is deceased as compared to a cell not contacted with said molecule (see column 11 lines 40-65 and column 13), wherein the S. cerevisiae cell is a cell that recombinantly expresses said target polynucleotide sequence (see column 1 lines 5-10), wherein said contacting is carried out in a liquid high throughput-like assay (see column 2 lines 10-25), wherein the S. cerevisiae cell is a cell that recombinantly expresses said target polynucleotide sequence (see column 1 lines 5-10), wherein said contacting is carried out in a liquid high throughput-like assay (see column 2 lines 10-25).

Dixon et al teach that the activity of the reporter gene when grown under aerobic conditions in the absence of inhibitors of sterol biosynthesis is low which correlates to a method

wherein RNA expression of said polynucleotide is changed in said cell contacted with said molecule as compared to a cell not contacted with said molecule (see columns 5 last lines and column 6). Dixon et al teach the reporter strain described in Example 1, in which the promoter of an acetoactyl CoA thiolase gene is linked to a reporter gene, inhibition of sterol biosynthesis results in stimulation of reporter gene output and reporter gene output allows further definition of the promoter elements which mediate the response to reductions in sterol levels which correlates to a method, wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule is increased as compared to a cell not contacted with said molecule.

Dixon et al teach cells which contain mutations, such as cell wall mutations, which increase the permeability of the fungal cell wall to compounds and other exogenous agents. Such mutations may be selected by mutagenising a reporter strain such as that described in Example 1, and selecting cells which show an enhanced response to sterol biosynthesis inhibitors which correlates to a method, wherein said altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule is increased as compared to a cell not contacted with said molecule.

Dixon et al teach reporter cells containing the ACoAT-based reporter gene which may also contain mutations or other additional genes which alter the rate of flux through the sterol biosynthesis pathway and hence alter the sensitivity of the assay to sterol biosynthesis inhibitors (see column 4 lines 1-25 and column 8 lines 1-15) which correlates to a method wherein an altered level of RNA expression or protein expression of said polynucleotide in said cell contacted with said molecule as compared to a cell not contacted with said molecule indicates that said function or activity of said sterol biosynthesis pathway is altered.

Dixon et al teach in vivo assays for inhibitors of sterol biosynthesis wherein inhibition leads to a change in the level of expression of a reporter gene and nucleic acids and recombinant cells use in the assays (see column 1). Dixon et al teach a method, wherein marker gene is chloramphenicol acetyl transferase (column lines 50-65), wherein said molecule is of natural products (see column 1 lines 5-10), wherein said contacting comprises incubating said cell with a second cell that produces said molecule, wherein said molecule is released by said second cell, wherein said molecule is secreted by said test second cell (column 11).

Conclusion

5. No claims are allowed.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/
for Nina Archie, Examiner of Art Unit 1645